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Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
(302) 774-6443

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ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment, See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not.exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).
- o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.
- othe "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

- othe "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.
- othe "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g,* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See,* 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy",43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide.*

TEST TYPE	1978 POLICY CRITERIA EXIST?	New 1991 GUIDE CRITERIA EXIST?
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	}[6]	}[7]
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y[8]
SKIN SENSITIZATION (ANIMALS)	N	Y[9]
EYE IRRITATION	N	Y[10]
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y[11]
REPRODUCTION STUDY	N	Y[12]
DEVELOPMENTAL TOX	Y[13]	Y[14]

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[6] 43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporitng of specifiec effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemicalL unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[7] Guide at pp.22, 29-31.

[8] Guide at pp-34-36.

[9] Guide at pp-34-36.

[10] Guide at pp-34-36.

[11] Guide at pp-22; 36-37.

[12] Guide at pp-22

[13] 43 Fed Reg at 11112

"Birth Defects" listed.

[14] Guide at pp-22

NEUROTOXICITY	N	Y[15]
CARCINOGENICITY	Y[16]	Y[17]
MUTAGENICITY		
In Vitro	Y}[18]	Y} [19]
In Vivo	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y}[20]	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reprodcutive	N	N

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[15] Guide at pp-23; 33-34.

[16] 43 Fed Reg at 11112
"Cancer" listed

[17] Guide at pp-21.

[18] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

[19] Guide at pp-23.

[20] 43 Fed Reg at 11112; 11115 at Comment 16.

CAS# 56-35-9
CHEM: Tributyl tin oxide
TITLE: Clinical studies of materials impregnated with tributyl tin oxide
DATE: None
SUMMARY OF EFFECTS: Summary of studies assessing germicide properties of compound; rabbit skin damaged at 10 times "use" concentration.

CLINICAL STUDIES OF MATERIALS IMPREGNATED WITH TRIBUTYL TIN OXIDE

Practical realization of the concept of permanently fixed germicidal activity in materials has long been sought. Organic germicides cannot be fixed. All wash out on cleansing and practically all are irritating at effective concentrations. Metal germicides which can be permanently bonded are soon inactivated by oxidation, alkalis, or the sulfur compounds of organic matter. However, recently it has been shown that an organo-metallic compound - tributyl tin oxide (TBTO) - is apparently not only resistant to leaching and laundering but also able to retain its germicidal activity, even under adverse chemical conditions. The Permachem Corporation has developed a method of impregnating materials with this germicidal agent. Its efficacy has been established by extensive tests designed to show germicidal persistance under use conditions. Its safety in use has also been determined. Animal toxicity studies prefaced human patch and use tests. The analytical work (chemical and bacteriological) was done at the Battelle Memorial Institute (Columbus, Ohio) and at the Permachem Laboratories (West Palm Beach, Florida). Animal toxicology studies were made at the Hazleton Laboratories (Falls Church, Virginia). The human safety aspects from a dermatological standpoint were determined by Dr. Herbert J. Spoor and Lawrence B. Slobody and the Pediatricians at New York Medical College did the Clinical tests. This report presents primarily the clinical developmental work on tributyl tin oxide.

EFFICACY OF TRIBUTYL TIN OXIDE AS A GERMICIDE

If a germicide is to be fixed successfully to a specific fabric to make the fabric "self-sanitizing", "self-disinfecting" or "self-sterilizing", it must meet two requirements. It must not diffuse out under use conditions, but remain fixed to the fabric and it must retain its ability to kill on contact, micro-organisms presented to it. Tributyltin oxide met these requirements.

That it can be bound to fabric was shown when samples of the fabric were dyebeck treated in such a way that a given number of parts per million (PPM) of tributyl tin oxide based on the weight of cloth was in the dyebeck liquor. The cloth samples became impregnated with tributyl tin oxide. Spectrographic analysis (Battelle Memorial Institute) showed the degree of impregnation. Persistent presence of tributyl tin oxide after launderings was also shown. Table I gives the results obtained when the fabric was dyebecked at the level of 500 PPM of tributyl tin oxide [1].

1. Report April 2, 1957 (from R. S. Sobell)

CLINICAL STUDIED OF MATERIALS IMPREGNATED WI TH TRIBUTYL TIN OXIDE

SUMMARY

Tributyl tin oxide, an organo-metallic compound, has been incorporated into materials to give them fixed germicidal activity. Materials so impregnated have been subjected to washing and leaching experiments to show retention efficacy of the germicide, to animal toxicology studies and to human safety tests. Fabrics and plastics so processed and tested have been used clinically on a large series of pediatric patients to confirm efficacy and establish safety in use as wearing apparel. The wearing apparel consists of cotton shirts and pants, vinyl pants, and bibs. One hundred and one clinical case histories of hospitalized babies and children establish that the organo-tin fixed germicidal impregnation gives a product that is safe under the most drastic use conditions. Concomitant bacteriological assays on representative

CLINICAL STUDIES OF MATERIALS IMPREGNATED WITH TRIBUTYL TIN OXIDE

SUMMARY

Samples of products as they were being frequently worn and processed through many hospital launderings have shown that the germicidal activity originally imparted has persisted to a fair degree.

Report submitted from New York Medical College,
Department of Pediatrics:

/s/ Lawrence B. Slobody, M.D., Chrm.
Lawrence B. Slobody, M.D., Chrm.

Co-ordinated by: /s/ Herbert J. Spoor, M.D.
Herbert J. Spoor, Ph.D., M.D.

Date: March 31, 1958

TABLE 1

Number of Washings	PPM TBTO	PPM Sn
"As Treated"	350	140
5 Times	212	85
10 Times	150	60
15 Times	100	40
20 Times	75	30
25 Times	75	30

To improve retention during the laundering process, an additional binding agent (1.25% polyvinyl acetate resin) was added to the dyebeck liquor. Spectrographic assay showed the following results.

TABLE 2

Number of Washings	PPM TBTO	PPM Sn
"As Treated"	120	300
5 Times	60	150
10 Times	70	175
15 Times	40	100
20 Times	70	175
25 Times	100	250

Despite the discrepancy in results here, which may be explained in terms of variability in the polyvinyl acetate resin release from the cloth, it is apparent that tributyl tin oxide thus impregnated is more laundry resistant.

To determine how well tributyl tin oxide was able to retain its germicidal activity, was the next step in the development of this product. The usual agar plate inhibition zone techniques developed for antibiotic assay were not applicable here because of the non-diffusible nature of the germicide. Only those organisms in actual contact with the impregnated fabric would be killed, adjacent ones would not. Therefore, some modified technique was necessary. The possibility of pouring an agar plate, then streaking it over the hardened surface, rather than uniformly distributing the test organisms throughout the media by pouring a seeded plate, was explored. It proved reasonably satisfactory, for in this way, the surface layer of test organisms came into direct contact with the topically applied test sample, and if the material had any appreciable activity, growth under the cloth patch would be inhibited. This "streak plate" method has proved to be a fast and practical way of following the persistence of germicidal activity of a material as it is being subjected to launderings or any other leaching treatments. To substantiate the results obtained by the "streak plate" method, germicidal activity of the materials under investigation has also been checked by a modification, as outlined by Dr. Herbert J. Spoor[1], of the method of Hoffman, Yeager and Kaze,[2] the so-called "Camp Dietrich Test" for establishing asepsis of surfaces. Results by this more

stringent research technique have been comparable for the fabric materials under investigation. Therefore, the "streak plate method" has been considered satisfactory for fast measurement of efficacy of the fixed germicide. The procedure has been used throughout these studies as the routine bacteriological assay technique.

ANIMAL TOXICITY STUDIES

The toxicity studies on tributyl tin oxide were done by the Hazelton Laboratories. The work was designed to ascertain the exact animal toxicity of the compound, and is more fully presented in their reports. Briefly, however, the toxicity estimation consisted of acute oral, parenteral and chronic oral studies on three species of animals - two rodent and one non-rodent. First, a series of forty-eight hour rats were run at various feeding levels to establish the lethal dose for 50% of the animals (LD-50), then tributyl tin oxide was injected into rabbits to determine its LD-50 when used parenterally. Finally, chronic ninety day dog feeding studies were made. The necessary criteria for safety for tributyl tin oxide was thus established.

As a further measure of safety, leaching studies[3] were made on tributyl tin oxide. Although it had already been established in the efficacy studies that soap and water as used in laundering, did not readily leach out tributyl oxide, the leaching effects of simulated body fluids remained to be determined. Under the use conditions projected for the impregnated fabrics, the possibility of inadvertently leaching out deleterious quantities of tributyl tin oxide had to be considered. Impregnated wool (TBTO-300 PPM) and impregnated

1. Letter from Dr.Herbert J. Spoor to Mr.John Leach, Sept. 23, 1957
2. "Soap and Chemical Specialties", Volume 31, Number 8, 1955
3. Report - Hazelton Laboratories, July 15, 1957

cotton (TBTO-200ppm) were leached with the following solutions - distilled water (pH 7.0), lactic acid 1%, ammonia 1% and synthetic sweat; impregnated vinyl plastic (0.25 parts Permachem pp to 150 parts vinyl formulation - TBTO content 833ppm) was leached with urine (natural - preserved under toluene) in addition to the above four. Microbiological assays of these fluids after they had leached the treated materials were made against M.pyogenes aureus and C.albicans for tributyl tin oxide content. The investigators concluded that not more than 2-3% of the original impregnated tributyl tin oxide could be leached out by the test solutions. Therefore, inadvertent ingestion of toxic quantities of tributyl tin oxide from treated fabric or plastic could be considered a virtual impossibility.

Since tributyl tin oxide had been proved safe for use in all the preceding animal and laboratory studies, animal dermal studies were now in order, so as to establish levels at which these impregnated materials might properly be used in human patch testing. An experiment[1] was designed in which the shaved rabbit skin was to be given six three day exposures over a three week period, to materials impregnated with various quantities of tributyl tin oxide. The "use" concentration for impregnated vinyl was 0.25 parts Permachem pp to 150 parts vinyl formulation or 833 ppm TBTO. For impregnated cotton, it was to be 1236 ppm TBTO in one series, and 993 ppm TBTO plus 2% polyvinyl acetate as resin binder in another. At "use" concentrations, impregnated materials proved to be as non-irritating as the untreated controls. However, at the test level of ten times "use" concentration, the impregnated materials proved quite damaging to the rabbit skin.

1. Letter from Hazelton Laboratories to Mr.John Leach-Aug.26,1957

The highest reasonably well tolerated level was four times the "use" concentration.

HUMAN SAFETY TESTS

To determine the skin irritation-sensitization potential of Permachem impregnated fabrics in the human, the standard Schwartz-Peck Closed Patch (intact and abraded skin) and the Draize-Shelanski multiple insult tests were used. The Schwartz-Peck test consists of application of test material to a skin site for forty eight hours under a closed (water impervious) patch (Duke Elastopatch). In this way, primary irritation is measured. After an interval of two weeks, the same material is reapplied to the same skin site, again for forty eight hours, under a closed patch. If reactions are of greater severity than those on the irritation series, a sensitization potential can be predicted. In these experiments, both intact and intentionally abraded skin sites were exposed to the test materials. The skin was abraded so as to magnify insult to the dermis as well as to the epidermis, thus mimicing to a degree natural skin trauma. The Draize-Shelanski test is the human adaptation of the old Landsteiner[1] guinea pig intradermal test. In the human, it is done under closed patches rather than intradermally, but the timing is comparable. The test material is applied under closed patch for forty-eight hours to the same site every other day for nine applications. The patches remain in place for forty-eight hours, therefore, the test is actually one of continuous exposure to an agent which is refreshed every second day. This constitutes the multiple insult-irritation phase of the test. After the ninth or final

1. Landsteiner, K. and Jacobs, J.: J. Exp. Med. 61:643, 1935.

irritating application has been made and read, the skin is given a rest period of one week, then another patch is applied to the same site for forty-eight hours. This is the sensitization challenge. When reactions do occur, they are graded in the following ways:-

- No reaction
(/ Questionable Erythema
-
1/ Definite Erythema
2/ Erythema and Edema
3/ Erythema, Edema and vesiculation

A combination of one hundred Schwartz-Peck and twenty-five Draize-Melanski subjects constitutes a very stringent human skin test. Its severity is not duplicated in any normal use.

In studying the impregnated Permachem products, the Schwartz-Peck test was run on materials of several concentration levels. This material in its original form has been reported to the Company.[1] A summary of the results is tabulated below:

TABLE 3

SCHWARTZ-PECK RESULTS - IMPREGNATED PLASTIC

	Irritation			Sensitization		
1% Permachem PP	(/)	(/)	(2/)	(/)	(/)	(2/)
Intact skin	1	10	11	14	1	8
Abraded skin	1	10	11	14	0	9
.5% Permachem PP						
Intact skin	3	1	0	0	1	0
Abraded skin	3	1	0	0	1	0
.25% Permachem PP						
Intact skin	4	0	0	0	0	0
Abraded skin	1	0	0	0	0	0

The 0.25% Permachem PP concentration was considered safe for any conceivable use. The 0.5% Permachem PP material was considered safe for any practical use in wearing apparel.

1. Letters from Dr.Herbert J.Spoor to Mr.John Leach: April 3,1957
June 3,1957

TABLE 4

	Irritation			Sensitization		
350 ppm TBTO	(±)	(+)	(2+)	(±)	(+)	(2+)
Intact skin	0	0	0	0	0	0
Abraded skin	0	0	0	0	0	0
300 ppm TBTO						
Intact skin	0	0	0	0	0	0
Abraded skin	0	0	0	0	0	0
1236 ppm TBTO						
Intact skin	3	1	0	0	0	0
Abraded skin	1	0	0	3	0	0
933 PPM TBTO Plus 2% Polyvinyl acetate as r esin binder						
Intact skin	4	0	0	0	0	0
Abraded skin	1	0	0	2	0	0

The 1236 ppm TBTO and the 993 ppm TBTO plus 2% polyvinyl acetate as resin binder was considered safe.

The results of the Draize-Shelanski test (on twenty-six individuals) also showed the Permachem impregnated cloth to be safe. In this group, despite the fact that there were two hundred and thirty-four irritation exposures, only one individual showed one questionable erythema (±)reaction after the third exposure. Another subject showed a similar type of mild reaction after the eighth exposure. Neither of these reactions persisted nor recurred. No reactions, whatsoever, occurred in the s ensitization challenge, therefore, the mild irritations noted may b e classed as coincidental and not indicative of dermal irritation. Table 5 shows these results.

	Irritation	Sensitization
Exposures #'s	1 2 3 4 5 6 7 8 9	# 1
Reactions (From 26 Individuals)	0 0 1 0 0 0 0 1 0 (±) (±)	0

CLINICAL TRIAL -"USE TEST"

Once the patch tests had established the safety - in terms of skin irritation - of the impregnated Permachem materials, a complete clinical trial was in order. First, a preliminary wear test was made in Canada.[1] Clothing - hose, underwear, shirts and shorts, and diapers - were distributed to male and female workers in industrial plants and to their children for wear. In all, the various types of impregnated garments were worn by two hundred and twenty-two subjects. Of this group, four were babies, twenty-four were children of three to twelve years and thirty-six were women. The wear period lasted up to three months in some cases. Only four cases of irritation were reported in the entire group. Of these, one was a baby troubled with other complications and hence considered not a normal subject; the second was a woman who found the same garment of Helanca nylon just as irritating when it was not impregnated with tributyl tin oxide; and the remaining two were children who developed a rash, apparently from the underwear under particularly humid weather conditions. The rash, once it was resolved, did not reappear when wear of the shorts was resumed. This test also indicated that the germicidal efficacy of the garments persisted, as evidenced by the absence of ammoniacal odor in the diapers, and by continued absence of foot odors in cases (eighty-four individuals) where impregnated hose were worn.

1. Letter from Thomson Research Association Ltd. to Mr. John Leach - February 21, 1958

To further confirm the safety findings, a controlled clinical trial, under professional supervision, was initiated at the New York Medical College, Department of Pediatrics. In this test, pediatric patients wore vinyl plastic pants and bibs or cotton shirts and pants. The materials were identical in terms of quantity of impregnated tributyl tin oxide with those previously proved skin safe by patch tests. Upon admission to the hospital the test product (cotton shirt and pants or vinyl pants) was put on the subject. The subjects were unselected. The garment and size chosen depended upon the age and development of the child. Thereafter, the clothing was worn on a twenty-four hour basis throughout the patient's hospital stay. This ranged from a few hours to thirty-eight days. The median stay was approximately eight days. In cases where cotton shirts and shorts were worn, daily changes were made. Vinyl pants were changed twice daily. Bibs were used at all meals. The garments were laundered after every wearing. An effort was made to use the same garments on the same subject whenever possible. Admissions dated from November 7 to November 23 were given new unlaundered clothing. Those admitted between November 23 and January 2 were given clothing which had been laundered a known number of times. Representative samples of laundered clothing were shipped each week to the Permachem Laboratories for assay for germicidal activity. Table 6 shows the results thus obtained using the Streak Plate Method. After January 2, a new batch of unlaundered clothing was again available. It, too, was assayed after laundering. Table 6 shows that at the end of the

fourth week, (twenty-eight launderings of the cotton shirts and pants and vinyl pants, and fifty-six launderings of the bibs) there was a marked decrease indemonstrable bacteriostatic and fungistatic properties. However, continued laundering apparently restored some germistatic activity, for the samples submitted from the hospital after forty-two launderings of cotton shirts and pants and vinyl pants, and eighty-four launderings of bibs had regained this property. No explanation can be offered for this.

TABLE 6

Project Began November 7	Number of Washings	M.aureus	B.subtilis	T.gypseum	A. niger	C.globosum	M.verrucaria
Week Ending November 14:							
Cotton pants	7	-	-	-	-	-	-
Cotton shirts	7	-	-	-	-	-	-
Vinyl pants	7	-	-	-	-	-	-
Vinyl bibs	14	-	-	-	-	-	-
Week Ending November 21:							
Cotton pants	14	-	-	-	-	-	-
Cotton shirts	14	-	-	-	-	-	-
Vinyl pants	14	-	-	-	-	-	-
Vinyl bibs	28	-	-	-	-	-	-
Week Ending November 28:							
Cotton pants	21	f	f	-	-	-	-
Cotton shirts	21	f	f	sl.f	sl.f	-	-
Vinyl pants	21	-	-	-	-	-	-
Vinyl bibs	42	-	-	-	-	-	-
Week Ending December 6:							
Cotton pants	28	ff	ff	ff	ff	-	-
Cotton shirts	28	ff	ff	sl.f	f	-	-
Vinyl pants	28	-	-	-	-	-	-
Vinyl bibs	56	-	-	-	-	-	-
Week Ending December 13:							
Cotton pants	35	fff	fff	fff	fff	-	-
Cotton shirts	35	fff	fff	sl.f	ff	-	-
Vinyl pants	35	-	-	-	-	sl.f	-
Vinyl bibs	70	sl.f	sl.f	-	-	-	-

Week Ending December 27:							
Cotton pants	42	sl./	sl./	sl./	sl./	sl./	sl./
Cotton shirts	42	sl./	sl./	sl./	sl./	sl./	sl./
Vinyl pants	42	-	-	-	-	-	-
Vinyl bibs	84	-	-	-	-	-	-
Week Ending January 3:							
Cotton pants	49	-	-	sl./	sl./	-	-
Cotton shirts	49	-	-	-	-	-	-
Vinyl pants	49	-	-	-	-	/	/
Vinyl bibs	98	-	-	-	-	/	/
Week Ending January 10:							
Cotton pants	7	-	-	-	sl./	-	-
Cotton shirts	7	-	-	sl./	sl./	sl./	sl./
Vinyl pants	7	-	-	-	-	-	-
Vinyl bibs	14	-	-	-	-	-	-
Week Ending January 17:							
Cotton pants	14	-	-	-	-	-	-
Cotton shirts	14	-	-	-	-	-	-
Vinyl pants	14	-	-	sl./	-	sl./	sl./
Vinyl bibs	28	-	-	-	-	-	-

Legend: sl./ - very slight growth around the edge
/ - 5-10% overgrowth
// - 40% overgrowth
/// - 70% overgrowth

A summary of the number of patients that initially wore garments laundered the various number of times, is given in Table 7 - for, as stated earlier, all patients did not start on unlaundered garments. Many had their first exposure to clothing that had been laundered many times.

TABLE 7

TYPE OF GARMENT USED FOR FIRST EXPOSURE	NUMBER OF CASES	
Unlaundered	53	
Laundered 1-7 times	1	
Laundered 7-14 times	0	
Laundered 14-21 times	6	
Laundered 21-28 times	11	- Bacteriostatic activity lost
Laundered 28-35 times	10	
Laundered 35-42 times	9	- Bacteriostatic activity regained
Laundered 42-56 times	11	

The total number of children studied was one hundred and one. They represented the typical admissions of a large city hospital - infections, accidents, emergency newborns and functional disorders. They ranged in age from the newborn to ten years. The age distribution is presented in the tabular summary, about 25% were infants, 27% were pre-nursery, 28% pre-school and 20% school age. The entire group wore one hundred and ninety-one garments two thousand and thirty-two times. The type of garment, the age group by which it was worn, and the number of wearings that it received and the number of launderings that it had, is presented in tabular form - Table 8.

TABLE 8

Summary of Clinical Data

Duration of Study:	November 7, 1957 to January 17,1958 - ten weeks	
Number of Children:	One hundred and one (101) -	thirty-three female, sixty-eight male
Age range:	Newborn to ten (10) years	
Age distribution:	Under one year - 26	
	One to three years - 27	
	Three to six years - 28	
	Six to ten years - 20	
	101	

Number of Each Type of Garment Worn by Each Age Group

	Under 1	1-3 Years	3-6 Years	6-10 years	Total
Cotton pants	2	24	27	20	73
Cotton shirts	1	26	28	20	75
Vinyl pants	25	5	0	0	30
Vinyl bibs	12	1	0	0	13
	40	56	55	40	191

Number of Times Each Age Group Wore Each Type of Garment

	Under 1	1-3 Years	3-6 Years	6-10 Years	Total
Cotton pants	22	225	195	122	564
Cotton shirts	11	234	202	122	569
Vinyl pants	522	32	0	0	554
Vinyl bibs	336	9	0	0	345
	891	500	397	244	2,032

The absence of irritation was impressive. In the entire group there were only three mild erythematous reactions. These were to the cotton shirts and pants. In all instances these reactions appeared within a few hours of the wearing of the garment. After the garment was removed, the reaction disappeared quickly and did not recur. The reactions were irritative phenomena. One reactor was a six year old female admitted for observation for ruptured spleen; another was a four year old male admitted for tonsillectomy. Both of these

wore the unlaundered cotton shirts and pants. The third was an eight month old male admitted for scrotal edema. He wore cotton shirts and pants, and vinyl pants. The irritation appeared only around the waist and was ascribed to the shirt. It is worthy of note, that in instances where reactions might logically have been expected, none occurred. A one and a half month old infant with severe diarrhea wore vinyl pants with no reaction. A three month old infant with urinary problems wore vinyl pants for thirty-five days with no reaction. Mentally retarded children with no control of excretory habits had no problem with this clothing. Leukemics with ulcerated lesions did not find it aggravating. An asthmatic, an inherently allergic individual, was not irritated. In instances of liver infection, pruritus was not induced, although these skins are extremely sensitive. Two cases of rash due to generalized eczema, present on admission, were not aggravated. The clothing was worn throughout the entire treatment period, and the rash cleared during the wearing. It did not recur on continued wear of the clothing. It might be well to mention that the cotton shirts and pants and the vinyl pants were so acceptable to household hospital staff, that theft was a serious problem. The vinyl bibs, on the other hand, were totally unacceptable because of their inability to absorb spillage. It was even difficult to obtain cooperation from the staff for their use.

All one hundred and one cases studied are summarized in this report. They follow on the succeeding pages.

Duration of Wear	Age	Sex	Type of Garment Worn	Date of Admission	Number of Launderings on garments initially worn	Diagnoses	Significant Comment
4 days	6 yrs.	M	S&P	11/15	New	T&A	
5 days	9 yrs.	M	S&P	11/9	New	Pneumonia	
6 days	4½ mths	F	VP&B	11/7	New	Respiratory infection	
11 days	2½ yrs	M	S&P	11/12	New	Pneumonia	
19 days	17 mths	M	S&P	11/29	22	Anemia	
	2 yrs	M	S&P	12/3	26	Bronchitis	
1	2½ yrs	F	S&P	1/2	56	Questionable growth	
19 days	13 mths	M	S&P	11/29	22	Hernia	
8 days	8 yrs	F	S&P	12/16	39	GI Infection	
5 days	13 mths	F	S&P	12/5	28	Eye Infection	
1 day	1½ mths	F	VP	11/7	New	Diarrhea & Vomiting	No Irritation
35 days	3 mths	M	VP	11/19	New	Urinary Problems	ditto
7 days	1 yr	M	S&P	11/7	New	Ear Infection	
3 days	7 yrs	M	S&P	11/24	17	Ear Infection	
4 days	3½ yrs	F	S&P	12/26	49	Respiratory Infection	
1 day	19 mths	F	S&P	12/23	46	Respiratory Infection	
8 days	8 yrs	M	S&P	12/15	38	Rheumatic Infection	
8 days	9 mths	F	VP	12/10	33	Hernias	

Duration of Wear	Age	Sex	Type of Garment Worn	Date of Admission	Number of Launderings on garments initially worn	Diagnoses	Significant Comment
28 days	2½ yrs	M	S&P	11/7	New	Tumors	
16 days	2 yrs	M	S&P	12/7	30	Tumors	
10 days	3 yrs	M	S&P	12/27	50	Hernia	
18 days	6 wks	F	VP&B	12/5	28	Pneumonia	
11 days	10 mths	M	P&B	11/7	New	Pneumonia	
[illegible]s	6 yrs	M	S&P	12/28	51	Bleeding GI tract	
18 days	Newborn	M	VP	11/24	17	Emergency Admission	
15 days	6 yrs	M	S&P	11/8	New	Questionable	
7 days	3 yrs	M	S	12/16	39	Pneumonia	
1 day	1 yr	M	VP	12/23	46		
2 days	6 yrs	M	S&P	11/21	New	Observation for Ruptured Spleen	Mild Irritation
8 days	4 mths	M	VP	11/19	New	Croup	
19 days	4 mths	M	VP	12/19	42	Asthma	
3 days	5 yrs	M	P&S	11/11	New	Respiratory	
13 days	3 yrs	F	P&S	11/7	New	Observation	
9 days	2 yrs	F	P&S	12/9	32	Hernia	
7 days	3½ yrs	F	P&S	11/20	New	Rheumatic Fever	
8 days	10 yrs	M	P&S	11/24	17	Pneumonia	
2 days	5 yrs	M	P&S	11/7	New	Ear Infection	
17 days	5 yrs	F	P&S	11/23	New	Growths	
17 days	3 yrs	F	S&P	11/7	New	Concussion	

Duration of Wear	Age	Sex	Type of Garment Worn	Date of Admission	Number of Launderings on garments initially worn	Diagnoses	Significant Comment
13 days	15 mths	M	S&P	11/8	New	Leukemia	
5 days	2 yrs	M	S&P	11/19	New	** Rash on admission	Not aggravated
5 days	Newborn	M	VP&B	12 ,29	52	Emergency Admission	
4 days	7 yrs	M	S&P	11/19	New	Pnuemonia	
? days	3 yrs	M	S&P	11/7	New	Ear Infection	
- ay	1½ mths	M	VP&B	12/1	24	Circumcision	
1 day	4½ yrs	M	S&P	12/29	52	T&A	
2 days	4 yrs	M	S&P	11/18	New	T&A	
4 days	4 yrs	M	S&P	11/7	New	GI Infection	
2 days	6 yrs	F	S&P	~~11~~/24	17	**Rash on admission	Not aggravated
2 days	4 yrs	M	S&P	12/18	41	T&A	
6 days	5 mths	M	VP	1/5	New	Liver Infection	No itch
4 days	4 yrs	M	S&P	11/27	20	Eye Infection	
13 days	3 yrs	F	S&P	11/23	New	Mentally retarded- Urinated uncontrolably	No Irritation
3 days	9 yrs	F	S&P	11/19	New	Appendectomy	Worn thru-out
3 days	1½ yrs	F	S&P	11/17	New	Pneumonia	
1 day	2½ yrs	M	S&P	11/23	New	Hernia	
3 days	16 mths	M	S,P,VP	12/2	25	Convulsions	
3 days	4½ yrs	F	S&P	11/7	New	Anemia	

* Rash appeared within 2 hours. Garment removed. Disappeared within 2 hrs.
** Cleared while clothing was being worn. Did not recur.

Duration of Wear	Age	Sex	Type of Garment Worn	Date of Admission	Number of Launderings on garments initially worn	Diagnoses	Significant Comment
11 days	6 yrs	F	S&P	11/7	New	Urinary tract bleeding	
8 days	4 yrs	M	S&P	11/18	New	Hernias	
6 days	13 mths	M	S&VP	11/20	New	Hernias	
13 days	8 yrs	F	S&P	1/2	25	Kidney abcesses	
days	8 mths	M	VP	11/10	New	Mental retardation	
2 days	5 yrs	M	S&P	11/9	New	T&A	
8 days	5 yrs	M	S&P	11/25	18	Eye surgery	
26 days	3 yrs	M	S&P	1/2	25	G.I. Infection	
1 day	3 yrs	M	S&P	11/18	New	G.I. Infection	
3 days	6½ yrs	F	S&P	11/20	New	Meningitis	
3 days	13 mths	M	S,VP,B	12/11	34	Convulsions	
7 days	10 yrs	M	S&P	11/8	New	Eye trouble	
5 days	9 yrs	M	S&P	11/13	New	Intestinal growth	
30 days	5 wks	M	VP	11/7	New	Birth paralysis	
38 days	2 yrs	F	S&P	12/8	31	Questionable pneumonia	
3 days	1½ yrs	M	S&P	12/27	50		
14 days	5 yrs	M	S&P	11/10	New	Leukemia	No aggravation to ulcerating lesion
1 day	4 yrs	M	S&P	11/7	New	Tonsillectomy	Mild Irritation
3 days	Newborn	F	VP&B	12/1	24	Emergency admission	

Duration of wear	Age	Sex	Type of Garment Worn	Date of Admission	Number of Launderings on garments initially worn	Diagnoses	Significant Comment
7 days	10 mths	M	VP&B	11/29	22	Pneumonia	
14 days	9 mths	F	VP&B	11/14	New	Convulsions	
4 days	1 yr	M	S&P	12/10	33	Hernia	
7 days	9 mths	F	VP&B	11/11	New	Pneumonia	
6 days	4 mths	M	VP&B	11/14	New	Chest Abcesses	
[illegible]ys	3 wks	F	VP	12/18	41	Blood crisis	
[illegible]ys	4 mths	M	VP	12/14	37	Circumcision	
10 days	5 yrs	M	S&P	12/16	39	Leukemia	No aggravation
7 days	9 yrs	M	S&P	12/9	32	T&A	
14 days	22 mths	M	S&P	12/17	40	Barrel chest	
3 days	27 mths	F	S&P,VP	1/5	3	Mentally retarded	
3 days	4 yrs	M	S&P	11/7	New	Nose bleeds	
4 days	15 mths	M	S&P	11/7	New	Mongoloid	
4 days	Newborn	M	VP&B	12/10	33	Emergency admission	
3 days	18 mths	F	S&P	11/7	New	Croup	
10 days	3 yrs	F	S&P	11/7	New	Meningitis	
7 days	8 mths	F	VP	11/28	21	Bronchitis	
5 days	10 yrs	M	S&P	12/18	41	Hernia	
5 days	11 mths	M	VP	11/19	New	2nd & 3rd Degree burns	
30 days	7 wks	F	VP&B	12/19	42	Mentally retarded	
3 days	8 yrs	F	S&P	11/7	New	Jaw swelling	

Duration of Wear	Age	Sex	Type of garment worn	Date of Admission	Number of Launderings on garments initially worn	Diagnoses	Significant Comment
3 DAYS	5 yrs	M	S&P	11/11	New	Hernia	
8 days	18 mths	M	S&P	11/8	New	Hernias	
11 days	8 mths	M	S&P,VP	11/29	22	Scrotal swelling	Mild Irritation *

Rash disappeared in 3-4 hours.

Triage of 8(e) Submissions

Date sent to triage: 5/28/96 NON-CAP (CAP)

Submission number: 12086A TSCA Inventory: (Y) N D

12086
Tributyl tin oxide, TBT,
CAS 56-35-9

Low

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

(ATOX) SBTOX (SEN) w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX (CTOX) (EPI) RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.):

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTR

A commercial use of tributyl tin oxide (TBT) as a permanently fixed germicidal in clothes was conceived (circa 1955-57) by a company other than the submitter. TBT is highly toxic to some organisms. 4 of 222 subjects in a loosely designed human trial in Canada experienced irritation. Used in marine paints, TBT has an extensive OPP file.

For Contractor Use Only

entire document: 0 1 (2) **pages** 1,9 **pages** _____

Notes:

Contractor reviewer: JW **Date:** 1/17/96

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ-1092-12086 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

SUB. DATE: 10/15/92 OTS DATE: 10/27/92 CSRAD DATE: 08/18/95

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)
DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME:

CAS#
56-35-9

INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
0202	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243	CHEM/PHYS PROP	01 02 04
0204	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCC/REL/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INCI OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
0208	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQEST DELAY	01 02 04	(0248)	PROD/USE/PROC	01 02 04
0209	NEURO (ANIMAL)	01 02 04	0224	PROD/COMP/CHEM ID	01 02 04	0251	MSDS	01 02 04
(0210)	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
(0212)	ACUTE TOX. (ANIMAL)	01 02 04	(0227)	ALLERG (HUMAN)	01 02 04			
0213	SUB ACUTE TOX (ANIMAL)	01 02 04	0228	ALLERG (ANIMAL)	01 02 04			
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
(0215)	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

TRIAGE DATA:	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	(YES)	YES (DROP/REFER)	RBT	LOW	germicide	
CAS SR	NO	NO (CONTINUE)	Rat	MED		
	DETERMINE	REFER:	Dog	HIGH		

COMM

12086 Tributyl tin oxide, TBT, CAS 56-35-9	Low	A commercial use of tributyl tin oxide (TBT) as a permanently fixed germicidal in clothes was conceived (circa 1955-57) by a company other than the submitter. TBT is highly toxic to some organisms. 4 of 222 subjects in a loosely designed human trial in Canada experienced irritation. Used in marine paints. TBT has an extensive ODR file.

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 1092 - 18506 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

SUB. DATE: 10/15/92 OTS DATE: 10/27/92 CSRAD DATE: 08/18/95

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

BEST COPY AVAILABLE

CHEMICAL NAME:

CAS#
56-35-9

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
(0210)	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
(0212)	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
(0215)	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
(0227)	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
(0248)	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA: NON-CBI INVENTORY
(YES)
CAS SR NO
DETERMINE

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER:

SPECIES
RBT
Rat
Dog
HMN

TOXICOLOGICAL CONCERN:
(LOW)
MED
HIGH

USE: germicide

PRODUCTION:

COMMENTS:

Tributlin fluoride impregnated in clothing material was tested for its dermal irritation & sensitization properties in rabbits & humans at 833 ppm & 1236 ppm. The Compound Showed lack of skin irritation & sensitization under these test Conditions

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 1092 - 18886 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

SUB. DATE: 10/15/92 OTS DATE: 10/27/92 CSRAD DATE: 08/18/95

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME: CAS# 56-35-9

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
(0210)	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
(0212)	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
(0215)	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
(0227)	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
(0248)	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA:

NON-CBI INVENTORY: (YES) / NO / DETERMINE

ONGOING REVIEW: YES (DROP/REFER) / NO (CONTINUE) / REFER:

SPECIES: RBT, Rat, Dog, HMN

TOXICOLOGICAL CONCERN: LOW / MED / (HIGH) – dermal irr./sens. in humans / (NO) – dermal irr. in rabbits

USE: germicide

PRODUCTION:

CAS SR

COMMENTS:

12086A

ND

Dermal irritation concern in rabbits could not be determined due to lack of adequate information for dose conversion. Rabbits received six 3-day exposures over a 3-week period to materials impregnated with the test substance. At "use" concentrations (833 ppm in impregnated vinyl and 993 or 1,236 ppm in impregnated cotton) no irritation occurred. A level ten times the "use" concentration was "quite damaging" to rabbit skin. The highest reasonably well-tolerated level was four times the "use" concentration.

H

Dermal irritation and sensitization in humans are of high concern. The skin irritation-sensitization potential of fabrics impregnated with the test substance were assessed in humans using the Schwartz-Peck Closed Patch test (48-hour initial dermal exposure and 48-hour challenge dermal exposure after two-week rest period) and the Draize-Shelanski multiple insult test (nine consecutive 48-hour exposures). One hundred subjects participated in the Schwartz-Peck test. For a 1% solution, 21 subjects exhibited irritation, and 9 subjects had a positive sensitization response. For a 0.5% solution, one subject exhibited irritation, and one subject had a positive sensitization response. A 0.25% solution did not cause irritation or sensitization. Twenty-six subjects participated in the Draize-Shelanski test. Two individuals exhibited questionable reactions, one after the third exposure and one after the eighth exposure.